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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,744	03/25/2005	Noboru Maki	053466-0395	7902

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,744	MAKI ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to the amendment filed March 14, 2008. Claims 1-21 are pending. Claims 1-6 and 21 have been amended. Claims 7-20 have been withdrawn as non-elected.

2. Claims 1-6 and 21 are considered in this Office action.

Claim Objection

3. (**Prior objection-withdrawn**) The objection to Claim 4 **is withdrawn** in view of amendment to the claim.

35 USC § 101 Utility

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. (**Prior rejection –withdrawn**) The rejection of Claims 1-4 under 35 U.S.C. 101, as the claimed invention is directed to non-statutory subject matter, **is withdrawn** in view of the amendment to the claims.

Claim Rejections - 35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. (**Prior rejection-withdrawn**) The rejection of Claims 1 and 3-6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention, **is withdrawn** in view of the amendment to Claim 1.

Claim Rejections - 35 USC § 112, first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. (**Prior rejection-withdrawn in part and maintain in part**) The rejection of Claim 1 under 35 U.S.C. §112, first paragraph, as lacking written description of the signal sequence requirement **is withdrawn** in view of the amendment to Claim 1. The rejection of Claim 4 under 35 U.S.C. §112, first paragraph, as lacking written description of HBV like particle comprising precore protein, is **maintained** for the reasons of record.

In response to Applicant's argument:

10. Applicant argues that one skilled in the art would have know of the *existence per se* of hepatitis B virus-like particles lacking DNA, as evidenced by Sakamoto *et al.,* Laboratory Investigation, 48:678-682 (1983) ("Sakamoto"). Specifically, Sakamoto describes that, among Dane particles, there are empty particles containing no DNA. The instant specification, pg. 4. Figure 3 of the application, which illustrates fractionation results of HBcrAg (the claimed "HBV core-like particle"), HBcAg, HBV-DNA, and

HBsAg. See also, specification, pp. 18-19.

11. Applicant's argument is not convincing because neither Sakamoto nor the cited specification teaches an HBV virus-like particle comprising precore protein. Saksmoto teaches HBV core like particle, not an HBV virus like particle comprising a precore protein. As indicated in the previous Office action, the prior art does not teaches that a precore protein is incorporated into an HBV particle (See e. g. Nassal, 1997, Figure 1A; and Schlicht, 1991, p. 6817). While the specification has disclosed that a precore protein can self-form a core like particle, it has not shown that the precore particle is assembled into HBV-like particle, nor any HBV-like particle that contain a precore protein. Because the specification lacks adequate description of HBV-like particle comprising a precore protein, which is not conventional to one of ordinary skill in the art, the rejection is maintained.

Claim Rejections - 35 USC § 112, first paragraph-Scope of Enablement

12. (**Prior rejection-maintained-extended**) The rejection of Claims 4 and 5 under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement (Scope of enablement), is **maintained** for the reasons of record, now is extended to Claims 1, 3, 5 and 6.

13. Claims 1, 3, 5 and 6 as amended are drawn to an isolated HBV precore protein that has an ability of forming core-like particles of HBV and that contains all or **part** of the signal sequence comprising amino acids at positions -29 to -11. However, the specification specifically indicates that a HBe antigen (a protein-processing product of

precore protein) comprising amino acid **-29** in its signal sequence does not form a core like particle, while a precore protein contains residue -28 in its signal sequence is able to form a core like particle, See e. g. Figure 1. Thus, the specification teaches that amino acid -29 in its signal sequence prevents the protein to form a particle. In view this teaching, the instant claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to make HBV precore protein that contains the signal sequence **-29** to -11 to forming core-like particles.

In response to Applicant's argument:

14. Applicant argue that Claims 4 and 5 are enabled because the specification teaches how to make HBV core like particle, and the art recognize the ability of using virus-like particles to treat hepatitis B.

15. This argument is not persuasive. Claim 4 lacks enablement requirement because the claimed HBV-like particle comprising the HBV procore protein is not adequately described by the specification. One of ordinary skill in the art would not know how to make it from the disclosure. The previous Office action has pointed out that an HBV core-like particle is not same as an HBV virus like particle. An HBV particle is composed by different viral proteins, but precore protein. Although the instant specification has disclosed HBV core-like particles, it has not taught one of skill in the art how to make and use a HBV virus like particle comprising precore protein.

16. Regarding Applicant's argument on Claim 5, just because the art may recognize that a virus-like particle could have potential use for treating hepatitis B infection, does not mean any virus-like particle is a vaccine, or a therapeutic agent, for any unknown application as claimed in Claim 5. The instant specification has not provided any teaching

regarding the clinical application of HBV precore protein. There is no any specific data in the specification showing that the HBV precore protein would be effective as a vaccine for any viral infections. As a result, the specification has not taught one of ordinary skill in the art how to use the alleged precore protein as a vaccine for any diseases. The rejection is maintained.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. **(Prior rejection-withdrawn in part and maintain in part)** The rejection of Claims 1, 2, 4-6 and 21 under 35 U.S.C. 102(b), as being anticipated by Takahashi (J. Immunology, 147(9): 3156-3160, 1991) **is withdrawn** in view of Applicant's argument and the amendment to the claims. The rejection of Claim 21 is maintained.

In response to Applicant's argument:

19. Applicant argues that Takahashi does not teach precore protein, $p20^e$, forms particles as claimed, and does not bind to antibodies raised against amino acids 19-29.

20. This argument is not convincing. Claim 21 does not require the precore protein in a form of particle, and does not require the precore protein to bind any specific antibody. Therefore, Applicant's argument is not relevant to Claim 21.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. (**Prior rejection-maintained**) The rejection of Claims 1-4 under 35 U.S.C. 103(a) as being unpatentable over Takahashi (J. Immunology, 147(9):3156-3160, 1991, cited in IDS), in view of Kobayash, **is maintained** for the reasons of record.

In response to Applicant's arguments:

23. Applicant argues that the obviousness rejection combining Takahashi and Kobayashi is improper because the teachings of the prior art is not consistent with the specification. Specifically, the HBe antigen described by Takahashi differs from the claimed HBV precore protein by two amino acids sequences. However, this difference produces HBe in free form but not in particle form, whereas the opposite is true of the claimed HBV precore protein. Thus, one skilled in the art would not have recognized that Kobayashi's teaching of an amino acid sequence that differs from the claimed sequence would have produced the claimed HBV precore protein, capable of forming virus-like particles.

24. This argument is not convincing. First, the prior art teaching is required to be consistent with the claim limitation, but not necessarily to the specification. Applicant argues the limitations that are not in the claims. Claim 1 is drawn to an isolated HBV

precore protein that **has an ability of** forming core-like particles of HBV and that contains all or part of the signal sequence comprising amino acids at positions -29 to -11 (Emphasis added). Please note that all HBV core antigen and HBe antigens are protein-processing products of an HBV precore protein. Takahash teaches p21c forms an HBV core-like particle. This teaching indicates that HBV precore protein of HBV (subtype adr), which contains **all** of the signal sequence at position -29 to 11, taught by Kobayash, **has an ability of forming** core-like particles of HBV. Therefore, the cited references meet the claim limitations.

25. Applicant further argues that there would be no reason for one skilled in the art to reasonably believe that the instant precore SEQ ID NO:1, which contains a mutation at position 119, would have produced a particle at all.

26. This argument is not persuasive, either. As shown in the previous Office action, the instant precore protein SEQ ID NO:1 differs from the precore protein of Kobayashi only by one amino acid change at position 119. As shown by Takahashi, it is the N-terminal signal sequence of a precore protein, but not the protein coding sequence, which is responsible for its ability to form a core-like particle. Takahashi teaches that precore products, p21c, p20, p18 and p17, have same coding sequence (subtype adr), but have different N-terminal signal sequences. Precore products p21c forms particle, whereas p20, p18 and p17 are in free forms. This prior art teaching is consistent with the instant specification, see e. g. Figure 1. Given the single amino acid change at coding region of HBV precore, one of ordinary skill would recognize it is a variant of HBV adr taught by Takahashi and Kobayashi.

"[W]hen one steps back and views the twisted structure of the protein as a whole, and considers the overall similarity of the protein of the prior art versus that coded for by the DNA claimed herein, and also considers the similarity of the DNA of the prior art versus that claimed herein, the minor change in the chemical configuration or design of the molecule discovered or made by appellants is so negligible that a *prima facie* case of obviousness exists. In legal parlance, on the record herein appellants' structural modification is *de minimis*." Ex parte Anderson, 30 USPQ2d 1866

27. Like the precore protein of HBV adr strain taught by Takahashi and Kobayashi, one of ordinary skill in the art would expect that the instant SEQ ID NO: 1 would have an ability of forming core like particles of HBV, since the instant SEQ ID NO: 1 contains the same signal sequence as that of HBV adr strain.

28. Since Applicant has not provided any compelling reasons to overcome the 103 rejection, the rejection is maintained.

Remarks

29. No claims are allowed. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Mary E Mosher, Ph.D./
Primary Examiner, Art Unit 1648

/Bo Peng/
Patent Examiner
July 7, 2008